S1 19 POLYANION? (S) PRODRUG?
S2 7 RD (unique items)
S3 427 OLIGO? (S) PRODRUG?
S4 45 S3 (S) TOXIC?
S5 15 RD (unique items)
S6 4 S3 (S) (POTENTIAT? OR SYNERG?)
S7 4 RD (unique items)
>>>KWIC option is not available in file(s): 41, 77, 399

7/3,K/1 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

06162126 EMBASE No: 1995170585
Synthesis and properties of phosphodiester and triester derivatives of AZT with tethered potential ribonucleases
Desseaux C.; Gouyette C.; Henin Y.; Huynh-Dinh T.
Unite de Chimie Organique, URA CNRS 487, Institut Pasteur, 28, Rue du Docteur Roux,75724 Paris Cedex France
Tetrahedron (TETRAHEDRON) (United Kingdom) 1995, 51/24 (6739-6756)
CODEN: TETRA ISSN: 0040-4020
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The synthesis of phosphate ester derivatives of AZT with tethered N,N,N'trimethylethylenediamine, N-methylpiperazine and 2,6-diacetyl pyridine as *prodrugs* of AZT with potential ribonuclease activity was described. The metal complexes of these compounds should combine a reverse transcriptase inhibition and the ability to hydrolyze...

...two chemical steps. The copper complexes of N,N,N'trimethylethylenediamine derivatives were fully characterized and their ribonuclease activity toward 25-mer and 28-mer *oligoribonucleotides* were demonstrated by capillary electrophoresis. The in vitro anti HIV preliminary assays revealed no *synergistic* effect with copper chelate on the activity of the *prodrugs*.

7/3,K/2 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

135313249 CA: 135(22)313249z JOURNAL
Potentiation of antitumor activity of irinotecan by chemically modified oligonucleotides
AUTHOR(S): Agrawal, Sudhir; Kandimalla, Ekambar R.; Yu, Dong; Hollister, Beth A.; Chen, Shih-Fong; Dexter, Daniel L.; Alford, Terri L.; Hill, Brenda ; Bailey, Karen S.; Bono, Christine P.; Knoerzer, Deborah L.; Morton, Phillip A.
LOCATION: Hybridon, Inc., Cambridge, MA, 02139, USA
JOURNAL: Int. J. Oncol. DATE: 2001 VOLUME: 18 NUMBER: 5 PAGES: 1061-1069 CODEN: IJONES ISSN: 1019-6439 LANGUAGE: English PUBLISHER: International Journal of Oncology

7/3,K/3 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

134361390 CA: 134(26)361390q PATENT
Polyanion co-administration for potentiation of prodrug efficacy
INVENTOR(AUTHOR): Agrawal, Sudhir
LOCATION: USA
ASSIGNEE: Hybridon, Inc.
PATENT: PCT International ; WO 200134093 A2 DATE: 20010517
APPLICATION: WO 2000US30687 (20001108) *US PV164182 (19991109)
PAGES: 26 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-000/A
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;

CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW ; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

7/3,K/4 (Item 1 from file: 149)

DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01422864 SUPPLIER NUMBER: 14144560 (USE FORMAT 7 OR 9 FOR FULL TEXT)

Anti-HIV properties of alpha-glucosidase inhibitor SC-48334, the active component of prodrug SC-49483. (Research Report)

Bryant, M.; Mueller, R.; Smidt, M.; Tiemeier, D.; Jacobs, G.; Platt, F.; Butters, T.; Karlsson, N.; Houseman, K.; Marr, J.

AIDS Weekly, p14(1)
July 26,
1993
PUBLICATION FORMAT: Newsletter ISSN: 1069-1456 LANGUAGE: English
RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 333 LINE COUNT: 00035

... 1993, in Berlin, Germany, "The N-linked glycans of the HIV envelope proteins are important for receptor binding, virus uptake and syncytia formation. Alteration of *oligosaccharide* addition, composition or processing leads to attenuation in HIV infectivity and cytopathicity due to aberrant folding, *oligomerization*, cleavage or transport of virion glycoprotein. SC-48334, n-butyl -deoxynojirimycin (BuDNJ), is an iminosugar which inhibits the endoplasmic reticulum a-glucosidase I resulting in biochemical modification of N-linked *oligosaccharides*. Inhibition of intestinal disaccharidases in vivo, however, can lead to carbohydrate malabsorption and diarrhea. *Prodrug* SC -49483 was developed to eliminate the GI side effects associated with oral administration of SC-48334. SC -49483 does not inhibit intestinal sucrase and...

...mononuclear cells, including monocytes/macrophages, infected with primary clinical isolates and AZT resistant strains of HIV. SC-48334, in combination with AZT or ddI, is *synergistic*; in combination with inhibitors of the late stages in virus replication (e.g., protease inhibitors) it is at least additive. Virion-associated glycoprotein from treated...
?

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(c) 2002 Thomson Derwent & ISI
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(c) 2001 DECHEMA
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(c) 2002 Reed Business Information Ltd.
File 370:Science 1996-1999/Jul W3
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File 399:CA SEARCH(R) 1967-2002/UD=13623
(c) 2002 AMERICAN CHEMICAL SOCIETY
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(c) 1998 Inst for Sci Info
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File 68:Env.Bib. 1972-2002/Apr
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(c) 2001 Informania Ltd.
File 787:Archives of Dermatology 1982-2002/May
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Set	Items	Description
S1	19	POLYANION? (S) PRODRUG?
S2	7	RD (unique items)
S3	427	OLIGO? (S) PRODRUG?
S4	45	S3 (S) TOXIC?
S5	15	RD (unique items)
S6	4	S3 (S) (POTENTIAT? OR SYNERG?)
S7	4	RD (unique items)

```
?s polyanion? (s) prodrug?
          19263  POLYANION?
          49361  PRODRUG?
      S1     19  POLYANION? (S) PRODRUG?
?rd
...completed examining records
      S2      7  RD (unique items)
?show files;ds;t/3,k/all
File   5:Biosis Previews(R) 1969-2002/May W4
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         (c)2002 Japan Science and Tech Corp(JST)
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         (c) 2002 The HW Wilson Co
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File 399:CA SEARCH(R) 1967-2002/UD=13623
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File  41:Pollution Abs 1970-2002/Jun
         (c) 2002 Cambridge Scientific Abstracts
File  50:CAB Abstracts 1972-2002/Apr
         (c) 2002 CAB International
File  68:Env.Bib. 1972-2002/Apr
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File  77:Conference Papers Index 1973-2002/May
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File 91:MANTIS(TM) 1880-2002/Jun
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Set	Items	Description
S1	19	POLYANION? (S) PRODRUG?
S2	7	RD (unique items)

>>>KWIC option is not available in file(s): 41, 77, 399

2/3,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10703183 BIOSIS NO.: 199799324328
Synthesis, conformation, biodistribution, and hormone-related in vitro antitumor activity of a gonadotropin-releasing hormone antagonist-branched polypeptide conjugate.
AUTHOR: Mezo Gabor; Mezo Imre; Pimm Malcolm V; Kajtar Judit; Seprodi Janos; Teplan Istvan; Kovacs Magdolna; Vincze Borbala; Palyi Istvan; Idei Miklos ; Szekerke Maria; Hudecz Ferenc(a)
AUTHOR ADDRESS: (a)Res. Group Peptide Chem., Hungarian Acad. Sci., Eotvos L. Univ., P.O. Box 32, H-1518 Budapest 11**Hungary
JOURNAL: Bioconjugate Chemistry 7 (6):p642-650 1996
ISSN: 1043-1802
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: microcapsules) for GnRH derivatives. Alternatively, these compounds can be covalently coupled to high-molecular mass carrier molecules for the design of bioconjugates acting as (a) *prodrugs* producing prolonged release or (b) macromolecular therapeutics. In order to evaluate the feasibility of this approach, a prototype construct has been prepared with a potent...
...Ala-m)) (XAK) type polypeptides with poly(L-lysine) backbone has been used in which X is an acetylated derivative of glutamic acid (AcEAK). This *polyanionic* polypeptide with free gamma-carboxyl groups was conjugated to MI-1544, which has only a single amino group at position 6. In this paper, we...

2/3,K/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10568576 BIOSIS NO.: 199699189721

Development of drug delivery systems for macromolecular drugs.
AUTHOR: Takakura Yoshinobu
AUTHOR ADDRESS: Fac. Pharmaceutical Sci., Kyoto Univ., 46-29 Yoshida-Konoe-cho, Sakyo-ku, Kyoto 606-01**Japan
JOURNAL: Yakugaku Zasshi 116 (7):p519-532 1996
ISSN: 0031-6903
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Japanese; Non-English
SUMMARY LANGUAGE: English

...ABSTRACT: pharmacokinetic characteristics of macromolecules in relation to their physicochemical properties such as molecular weight and electric charge. Based on this information, we first developed macromolecular *prodrugs* as a delivery system for low molecular weight drugs. An antitumor antibiotic, mitomycin C (MMC) were covalently conjugated with dextran and various types of macromolecular *prodrug* of MMC were developed for tumor targeting. Secondly, delivery systems for protein drugs such as soybean trypsin inhibitor, uricase, and recombinant superoxide dismutase (SOD) were...
...DNA. Prior to the development of delivery systems, we found that the pharmacokinetics of the nucleic acid drugs are decided by their physicochemical properties as *polyanions* even if these materials contain genetic information. Several approaches were tested to control the in vivo behavior of the oligonucleotides and plasmid DNA based on...

2/3,K/3 (Item 1 from file: 8)
DIALOG(R)File 8:Ei Compendex(R)

03363890 E.I. Monthly No: EI9201009983
Title: Polymer drugs and polymeric drugs. VIII. Slow release of 5-fluorouracil from *polyanionic* polymeric *prodrugs* containing 5-fluorouracil and their antitumor activity.
Author: Akashi, Mitsuru; Morita, Norikazu; Miyachi, Osamu; Yashima, Eiji; Miyauchi, Noriyuki; Minoda, Tomonori
Corporate Source: Kagoshima Univ, Kagoshima, Jpn
Source: New Polymeric Materials v 3 n 1 1991 p 31-39
Publication Year: 1991
CODEN: NPMAE8 ISSN: 0169-6424
Language: English

Title: Polymer drugs and polymeric drugs. VIII. Slow release of 5-fluorouracil from *polyanionic* polymeric *prodrugs* containing 5-fluorouracil and their antitumor activity.
...Abstract: fluorouracil (VBFU) were polymerized and copolymerized with vinyl monomers such as methacrylic acid (MA) and maleic anhydride (MAn) in the presence of AIBN to give *polyanionic* polymeric *prodrugs* containing 5-FU. The hydrolysis in a phosphate buffer solution and the antitumor activity of the polymeric *prodrugs* in Ehrlich's ascites or Sarcoma 180 ascites tumor-bearing mice were studied. (Author abstract) 12 Refs.
Identifiers: ANTITUMOR ACTIVITY; EHRLICH'S ASCITES; SARCOMA 180 ASCITES TUMOR-BEARING MICE; PHOSPHATE BUFFER SOLUTION; *POLYANIONIC* POLYMERIC *PRODRUGS*

2/3,K/4 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

07094459 PASCAL No.: 86-0254085
Polymeric *prodrugs*. IV: In vitro study of the drug release on a model p-nitroanilide bound onto *polyanionic* carrier
AZORI M; PATO J; FEHERVARI F; TUDOS F
Hungarian acad. sci., cent. res. inst. chemistry, Budapest 1525, Hungary
Journal: Makromolekulare Chemie, 1986, 187 (2) 303-309
Language: ENGLISH

Polymeric *prodrugs*. IV: In vitro study of the drug release on a model p-nitroanilide bound onto *polyanionic* carrier

2/3,K/5 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

134361390 CA: 134(26)361390q PATENT
Polyanion co-administration for potentiation of prodrug efficacy
INVENTOR(AUTHOR): Agrawal, Sudhir
LOCATION: USA
ASSIGNEE: Hybridon, Inc.
PATENT: PCT International ; WO 200134093 A2 DATE: 20010517
APPLICATION: WO 2000US30687 (20001108) *US PV164182 (19991109)
PAGES: 26 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-000/A
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW ; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

2/3,K/6 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

116181007 CA: 116(18)181007q JOURNAL
Effect of negative electric charges of polymers on the chymotrypsin catalyzed hydrolysis of the side chains
AUTHOR(S): Mora, M.; Pato, J.
LOCATION: Cent. Res. Inst. Chem., Hung. Acad. Sci., Budapest, Hung.
JOURNAL: J. Controlled Release DATE: 1992 VOLUME: 18 NUMBER: 2
PAGES: 153-8 CODEN: JCREEC ISSN: 0168-3659 LANGUAGE: English

2/3,K/7 (Item 1 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

07128956 Genuine Article#: A2428 No. References: 14
Title: POLYMERIC *PRODRUGS* .4. INVITRO STUDY OF THE DRUG RELEASE ON A MODEL PARA-NITROANILIDE BOUND ONTO *POLYANIONIC* CARRIER
Author(s): AZORI M; PATO J; FEHERVARI F; TUDOS F
Corporate Source: HUNGARIAN ACAD SCI,CENT RES INST CHEM,POB 17/H-1525 BUDAPEST//HUNGARY/
Journal: MAKROMOLEKULARE CHEMIE-MACROMOLECULAR CHEMISTRY AND PHYSICS, 1986 , V187, N2, P303-309
Language: ENGLISH Document Type: ARTICLE

Title: POLYMERIC *PRODRUGS* .4. INVITRO STUDY OF THE DRUG RELEASE ON A MODEL PARA-NITROANILIDE BOUND ONTO *POLYANIONIC* CARRIER
?

Set	Items	Description
S1	19	POLYANION? (S) PRODRUG?
S2	7	RD (unique items)
S3	427	OLIGO? (S) PRODRUG?
S4	45	S3 (S) TOXIC?
S5	15	RD (unique items)

>>>KWIC option is not available in file(s): 41, 77, 399

5/3,K/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

07975648 BIOSIS NO.: 000093043226

SYNTHESIS AND ANTITUMOR ACTIVITY OF ALPHA-1 4 POLYGALACTOSAMINE AND N ACETYL-ALPHA-1 4-POLYGALACTOSAMINE IMMOBILIZED 5 FLUOROURACILS THROUGH HEXAMETHYLENE SPACER GROUPS VIA UREA UREA BONDS

AUTHOR: OHYA Y; HUANG T Z; OUCHI T; HASEGAWA K; TAMURA J; KADOWAKI K; MATSUMOTO T; SUZUKI S; SUZUKI M
AUTHOR ADDRESS: DEP. APPLIED CHEM., FAC. ENG., KANSAI UNIV., SUITA, OSAKA, JPN.
JOURNAL: J CONTROLLED RELEASE 17 (3). 1991. 259-266. 1991
FULL JOURNAL NAME: Journal of Controlled Release
CODEN: JCREE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: In order to provide a macromolecular *prodrug* of 5-fluorouracil (5FU) with reduced side-effects, having an affinity for tumor cells and exhibiting strong antitumor activity, the covalent attachment of 5FUs to .alpha.-1, 4-polygalactosamine (PGA), N-acetyl-.alpha.-1, 4-polygalactosamine (NAPGA) and their *oligomers* (GOS, NAGOS) through hexamethylene spacer groups via urea, urea bonds was carried out. The survival effect against p388 lymphocytic leukemia in female CDF1 mice by ...

...showed significant growth-inhibitory effect on Meth-A fibrosarcoma. The obtained PGA/5FU, NAPGA/5FU, GOS/5FU and NAGOS/5FU conjugates did not display any *toxicity* even in the high dose ranges.

5/3,K/2 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

07952046 BIOSIS NO.: 000093031144

PLATELET AGGREGATION INHIBITING AND ANTICOAGULANT EFFECTS OF OLIGOAMINES XVI CYTOSTATIC AND CYTOTOXIC SIDE EFFECTS OF OLIGOAMINES

AUTHOR: REHSE K; NOACK B; MAURER R; HILGARD P
AUTHOR ADDRESS: INST. PHARMAZIE FREIEN UNIV., KOENIGIN-LUISE-STR. 2+4, D-1000 BERLIN 33, GER.
JOURNAL: ARCH PHARM (WEINHEIM) 324 (10). 1991. 797-802. 1991
FULL JOURNAL NAME: Archiv der Pharmazie (Weinheim)
CODEN: ARPMA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Selected synthetic *oligoamines* were able to inhibit (IC50) the growth of leukemic L 1210 cells in concentrations between 4-10 .mu.mol/L. The essential structural features were...

...cell nucleus could be observed this is most probably due to interaction with the cell membrane. When high local concentrations are applied in vivo, the *oligoamines* are *toxic* because of cytolytic properties. This *toxicity* can be overcome by administration of suitable *prodrugs* (LD50 > 1000 mg/kg).

5/3,K/3 (Item 1 from file: 8)

DIALOG(R)File 8:Ei Compendex(R)

03490272 E.I. Monthly No: EI9210122800
Title: Design of chitosan-5FU conjugate exhibiting antitumor activity.
Author: Ouchi, Tatsuro; Banba, Toshio; Masuda, Hiroshi; Matsumoto, Tatsuji; Suzuki, Shigeo; Suzuki, Masuko
Corporate Source: Kansai Univ, Suita, Jpn
Source: Journal of Macromolecular Science - Chemistry v A28 n 10 Oct 1991 p 959-975
Publication Year: 1991
CODEN: JMCHBD ISSN: 0022-233X
Language: English

Abstract: In order to provide a macromolecular *prodrug* of 5-fluorouracil (5FU) reducing the side effects, having an affinity for tumor cells, and exhibiting strong antitumor activity, the covalent attachments of 5FUs to chitosan and chitosamino-*oligosaccharide* (COS) through hexamethylene spacer groups via urea, urea bonds were carried out. The effect of prolongation of life was tested in vivo against p388 lymphocytic...

...showed remarkable growth-inhibitory effects on Meth-A fibrosarcoma and MH-134Y hepatoma. These chitosan-5FU and COS-5FU conjugates did not display an acute *toxicity* even in higher dose ranges. (Author abstract) 16 Refs.

5/3,K/4 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

10152300 Genuine Article#: 492WJ No. References: 56
Title: Defining a future role for radiogenic therapy
Author(s): Kaminski JM (REPRINT) ; Kaminski RJ; Dicker AP; Urbain JLC
Corporate Source: Med Coll Georgia,Dept Radiol,Augusta//GA/30912 (REPRINT); Med Coll Georgia,Dept Radiol,Augusta//GA/30912; Thomas Jefferson Univ Hosp,Dept Radiat Oncol,Philadelphia//PA/19107; Cleveland Clin Fdn,Dept Nucl Med,Cleveland//OH/
Journal: CANCER TREATMENT REVIEWS, 2001, V27, N5 (OCT), P289-294
ISSN: 0305-7372 Publication date: 20011000
Publisher: W B SAUNDERS CO LTD, 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND
Language: English Document Type: REVIEW (ABSTRACT AVAILABLE)

Abstract: The goal of cancer therapy is to eliminate the cancer and/or to arrest further growth while decreasing normal tissue *toxicity*, i.e. to increase the therapeutic ratio. This review focuses on a group of therapeutics that are either (I) directly stimulated by radiation to produce...

...indirectly cytotoxic agents (i.e. genes under the control of a radiation inducible promoter that produce a cytotoxic protein or an enzyme that converts a *prodrug* to an active form, respectively); (2) auger-electron emitting radiolabelled *oligonucleotides*, antibodies, nucleotide analogues, or other small molecules that are internalized; (3) radiation inducible genes that produce a ligand or transporter(or the like) which then...

5/3,K/5 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

09927383 Genuine Article#: 465RK No. References: 42
Title: Polymer-drug conjugates, PDEPT and PELT: basic principles for design and transfer from the laboratory to clinic
Author(s): Duncan R (REPRINT) ; Gac-Breton S; Keane R; Musila R; Sat YN; Satchi R; Searle F
Corporate Source: Univ Wales Coll Cardiff,Welsh Sch Pharm, Ctr Polymer

Therapeut,Redwood Bldg,King Edward 7 Ave/Cardiff CF10 3XF/S Glam/Wales/ (REPRINT); Univ Wales Coll Cardiff,Welsh Sch Pharm, Ctr Polymer Therapeut,Cardiff CF10 3XF/S Glam/Wales/
Journal: JOURNAL OF CONTROLLED RELEASE, 2001, V74, N1-3 (JUL 6), P135-146
ISSN: 0168-3659 Publication date: 20010706
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
Language: English Document Type: ARTICLE (ABSTRACT AVAILABLE)

...Abstract: stimulated significant interest in this field. Ongoing research is developing (1) conjugates containing drugs that could otherwise not progress due to poor solubility or uncontrollable *toxicity*; (2) conjugates of agents directed against novel targets; and (3) two-step combinations such as polymer-directed enzyme *prodrug* therapy (PDEPT) and polymer-enzyme liposome therapy (PELT) that can cause explosive liberation of drug from either polymeric *prodrugs* or liposomes within the tumour interstitium. Moreover, bioresponsive polymer-based constructs able to promote enclosomal escape and thus intracytoplasmic delivery of macromolecular drugs (peptides, proteins and *oligonucleotides*) are also under study.

5/3,K/6 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

09554870 Genuine Article#: 419UM No. References: 17
Title: Extracellularly tumor-activated prodrugs for the selective chemotherapy of cancer: Application to doxorubicin and preliminary in vitro and in vivo studies
Author(s): Trouet A (REPRINT) ; Passioukov A; Van Derpoorten K; Fernandez AM; Abarca-Quinones J; Baurain R; Lobl TJ; Oliyai C; Shochat D; Dubois V
Corporate Source: Univ Catholique Louvain,Cell Biol Lab,Pl Croix Sud 5/B-1348 Louvain//Belgium/ (REPRINT); Univ Catholique Louvain,Cell Biol Lab,B-1348 Louvain//Belgium/; Corixa,S San Francisco//CA/94080
Journal: CANCER RESEARCH, 2001, V61, N7 (APR 1), P2843-2846
ISSN: 0008-5472 Publication date: 20010401
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202 USA
Language: English Document Type: ARTICLE (ABSTRACT AVAILABLE)

Abstract: *Oligopeptidic* derivatives of anthracyclines unable to penetrate cells were prepared and screened for their stability in human blood and their reactivation by peptidases secreted by cancer cells. N-beta -alanyl-L-leucyl-L-alanyl-L-leucyl-doxorubicin was selected as a new candidate *prodrug*, The NH2-terminal beta -alanine allows a very good blood stability, A two-step activation by peptidases found in conditioned media of cancer cells ultimately yields N-L-leucyl-doxorubicin. In vitro, when MCF-7/6 cancer cells are exposed to the *prodrug*, they accumulate about 14 times more doxorubicin than MRC-5 normal fibroblasts, whereas when exposed to doxorubicin the uptake is slightly higher in fibroblasts than in MCF-7/6 cells. This increased specificity of the *prodrug* over doxorubicin was confirmed in cytotoxicity assays using the same cell types. In vivo, the *prodrug* proved about nine times less *toxic* than doxorubicin in the normal mouse and also much more efficient in two different experimental chemotherapy models of human breast tumors.

5/3,K/7 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08914569 Genuine Article#: 344VK No. References: 91
Title: Therapeutic developments in cytomegalovirus retinitis
Author(s): Hoffman VF (REPRINT) ; Skiest DJ
Corporate Source: PARKLAND HLTH & HOSP SYST,DEPT PHARM, 5201 HARRY HINES

BLVD/DALLAS//TX/75235 (REPRINT); UNIV TEXAS,SW MED CTR, DIV INFECT DIS/DALLAS//TX/75235
Journal: EXPERT OPINION ON INVESTIGATIONAL DRUGS, 2000, V9, N2 (FEB), P 207-220
ISSN: 1354-3784 Publication date: 20000200
Publisher: ASHLEY PUBL LTD, 1ST FL, THE LIBRARY, 1 SHEPHERDS HILL HIGHGATE, LONDON N6 5QJ, ENGLAND
Language: English Document Type: REVIEW (ABSTRACT AVAILABLE)

...Abstract: which may be more effective than either iv, ganciclovir or foscarnet, can also be used as a first line agent; however, it is associated with *toxicity* (renal and ocular) and thus needs careful use. Local therapy for CMV retinitis has been a significant advance. The intraocular ganciclovir implant has the highest efficacy of the approved agents and is well-tolerated. Fomivirsen, an *oligonucleotide* injected intravitreally, is a newly approved agent which offers alternative treatment. Intravitreal ganciclovir or foscarnet, although not approved, have been used successfully in some patients...

...those with recurrent or refractory disease. The development of new anti-CMV agents has been stalled by the decreased incidence of the disease. Valganciclovir, a *prodrug* of ganciclovir, offers excellent oral bioavailability and is the closest to approval of all the new anti-CMV drugs. High ganciclovir blood levels are achieved...

5/3,K/8 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

07426228 Genuine Article#: 164GY No. References: 41
Title: Macromolecular derivatives of N,N-di-(2-chloroethyl)-4-phenylene diamine mustard. 2. In vitro cytotoxicity and in vivo anticancer efficacy
Author(s): Soyez H; Seymour LW; Schacht E (REPRINT)
Corporate Source: STATE UNIV GHENT,DEPT ORGAN CHEM, POLYMER MAT RES GRP, KRIJGSLAAN 281 S4-BIS/B-9000 GHENT//BELGIUM/ (REPRINT); STATE UNIV GHENT,DEPT ORGAN CHEM, POLYMER MAT RES GRP/B-9000 GHENT//BELGIUM/; UNIV BIRMINGHAM,SCH MED, CRC, INST CANC STUDIES/BIRMINGHAM B15 2TT/W MIDLANDS/ENGLAND/
Journal: JOURNAL OF CONTROLLED RELEASE, 1999, V57, N2 (FEB 1), P187-196
ISSN: 0168-3659 Publication date: 19990201
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
Language: English Document Type: ARTICLE (ABSTRACT AVAILABLE)

Abstract: *Prodrugs* of N,N-di-(2-chloroethyl)-4-phenylene diamine (PDM) based on soluble poly[N-5-(2-hydroxyethyl)-L-glutamine] (PHEG) have been evaluated as...

...to exploit the enhanced permeability of tumour vasculature, combining a passive tumour tropism with systemic liberation of free PDM. Modification of PDM by coupling via *oligopeptide* spacers onto a polymeric carrier significantly reduced its cytotoxicity towards different cell types in vitro. On the other hand, incubation of the cells with the...

...this derivative. The PHEG-Gly-Phe-Ala-Leu-PDM conjugate, which is rapidly degraded by lysosomal and tumour-associated enzymes also showed a decreased systemic *toxicity* in vivo and could be administered at a dose of 8 mg PDM/kg body weight intravenously, compared with just 2 mg/kg for free...

5/3,K/9 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04338538 Genuine Article#: RV908 No. References: 43

Title: SYNTHESIS AND EVALUATION OF MACROMOLECULAR PRODRUGS OF MITOMYCIN-C
Author(s): DEMARRE A; SOYEZ H; SCHACHT E; SHOAIBI MA; SEYMOUR LW; RIHOVA B
Corporate Source: STATE UNIV GHENT,DEPT ORGAN CHEM,BIOMAT & POLYMER RES GRP,KRIJGSLAAN 281 S4-BIS/B-9000 GHENT//BELGIUM/; STATE UNIV GHENT,DEPT ORGAN CHEM,BIOMAT & POLYMER RES GRP/B-9000 GHENT//BELGIUM/; UNIV BIRMINGHAM,SCH MED,DEPT CLIN ONCOL/BIRMINGHAM B15 2TH/W MIDLANDS/ENGLAND/; ACAD SCI CZECH REPUBL,INST MICROBIOL/PRAGUE//CZECH REPUBLIC/
Journal: JOURNAL OF CONTROLLED RELEASE, 1995, V36, N1-2 (SEP), P87-97
ISSN: 0168-3659
Language: ENGLISH Document Type: ARTICLE (Abstract Available)

Abstract: Poly-[N-(2-hydroxyethyl)-L-glutamine] (PHEG) *prodrugs* of the antitumour antibiotic mitomycin C (MMC) were synthesised using peptidyl spacers, tri- and tetrapeptides, to link the drug to the macromolecular carrier. The relationship between the length and composition of the *oligopeptide* spacer and the rate of drug release was studied by incubation in buffers, serum and in the presence of enzymes (lysosomal enzymes and collagenase IV...
...leu conjugate released MMC very rapidly in the presence of both lysosomal enzymes and collagenase IV. Biological experiments indicate that PHEG-MMC conjugates act as *prodrugs* of MMC: cytotoxicity was observed after hydrolytic release of the active compound in vitro. In vivo studies of P388 solid tumour-bearing mice suggest that conjugates which release MMC slowly may be more effective in inhibiting tumour growth and prolonging animal lifespan. Preliminary in vivo bone marrow *toxicity* studies indicate that PHEG-MMC *prodrugs* are less myelosuppressive than free MMC.

5/3,K/10 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

01502121 2000174914
Emerging antibody-based HER2 (ErbB-2/neu) therapeutics
Krauss W.C.; Park J.W.; Kirpotin D.B.; Hong K.; Benz C.C.
ADDRESS: Dr. C.C. Benz, Division of Hematology-Oncology, University of California, Department of Medicine, 505 Parnassus Ave., San Francisco, CA 94143-1270, United States
EMAIL: benz@itsa.ucsf.edu
Journal: Breast Disease, 11/- (113-124), 2000, United States
CODEN: BRDIE
ISSN: 0888-6008
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 65

Targeting HER2(ErbB-2/neu) overexpressing tumor cells to selectively deliver anticancer agents and thereby reduce host *toxicity* represents a rational and emerging strategy for the treatment of breast and other epithelial cancers. The extracellular domain of the HER2 receptor tyrosine kinase is...

...to systemically administered antibody-based therapeutics, including growth-inhibiting monclonals such as rhuMAbHER2 (trastuzmab/Herceptin(C)) as well as anti-HER2 immunotoxins, antibody-dependent enzyme *prodrug* therapy (ADEPT), and immune cell recruiting bispecific antibodies. In addition to summarizing recent advances in these antibody-based strategies, this review focuses on preclinical advances...

...cancer, future applications of this novel targeting strategy will also broaden to include intracellular delivery of other anticancer agents as well as therapeutic nucleic acids (*oligonucleotides*, genes).

5/3,K/11 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

04467727 EMBASE No: 1990355836

Synthesis and antitumor activity of conjugates of 5-fluorouracil and chito-oligosaccharides involving a hexamethylene spacer group and carbamoyl bonds

Ouchi T.; Banba T.
Department Applied Chemistry, Faculty of Engineering, Kansai University,Suita, Osaka 564 Japan

Drug Design and Delivery (DRUG DES. DELIV.) (United Kingdom) 1990, 6/4 (281-287)
CODEN: DDDEE ISSN: 0884-2884
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

With the object of providing an *oligomeric* *prodrug* of 5-fluorouracil (5FU) with reduced side-effects, affinity for tumor cells and high antitumor activity, 5FU was covalently attached to three chito-*oligosaccharides* (COS) through hexamethylene spacer groups via carbamoyl bonds. The ability of these conjugates to prolong the life of lymphocytic leukemia mice (following their intraperitoneal administration...

...against the solid tumor than either 5FU, COS, or blends of 5FU and COS. At the highest dose levels, the conjugates did not cause acute *toxicity*, and did not cause rapid decrease in body weight.

5/3,K/12 (Item 1 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.

0177796 DBA Accession No.: 95-04617

Bioreversible analogs of oligonucleoside phosphorothioates: the S-acyloxyalkyl phosphorothiolates - stereospecific acyloxyalkyl phosphorothioate production using pig liver esterase; prodrug analog application in gene therapy (conference abstract)

AUTHOR: Iyer R P; Yu D; Agrawal S
CORPORATE AFFILIATE: Hybridon
CORPORATE SOURCE: One Innovation Drive, Worcester, MA 01605, USA.

JOURNAL: Clin.Chem. (40, 12, 2335) 1994
ISSN: 0009-9147 CODEN: CLCHAU
CONFERENCE PROCEEDINGS: The Genetic Revolution, San Diego, California, 17-19 November, 1994.
LANGUAGE: English

ABSTRACT: Phosphorothioate *oligonucleotides* (PS *oligos*) as sequence-specific inhibitors of gene expression have potential as therapeutic agents. R- and S-acyloxyalky dinucleoside phosphorothioates, were prepared by chemoselective alkylation with iodoalkyl...

... product (5%) were also observed. Enzyme-mediated anchimeric assistance in hydrolysis was proposed as a mechanistic basis for these results. Similar analogs, of other PS *oligos*, were also prepared which upon incubation with serum and esterases reverted to the parent *oligonucleotide* . The duplex of a derivatized 25-mer with a complementary RNA was less stable (51 deg) than that of the parent 25-mer, an active anti-HIV virus agent, (71 deg). No *toxicity* was observed with the parent 25-mer for 48 hr (3H-thymidine uptake) in H9 cells, up to a dose of 10 ug/ml. These *prodrug* analogs of PS *oligos* have potential as improved therapeutic agents. (0 ref)

5/3,K/13 (Item 1 from file: 149)

DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01488235 SUPPLIER NUMBER: 15765702 (USE FORMAT 7 OR 9 FOR FULL TEXT)

Gene therapy for vascular smooth muscle cell proliferation after arterial injury.
Ohno, Takeshi; Gordon, David; San, Hong; Pompili, Vincent J.; Imperiale, Michael J.; Nabel, Gary J.; Nabel, Elizabeth G.
Science, v265, n5173, p781(4)
August 5,
1994
PUBLICATION FORMAT: Magazine/Journal ISSN: 0036-8075 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Academic
WORD COUNT: 4040 LINE COUNT: 00322

... were minimal.
Taken together, these data suggest that introduction of a replication-deficient adenoviral vector encoding herpesvirus tk limits intimal hyperplasia after balloon injury. This *prodrug* approach, in which high levels of recombinant tk gene are expressed locally, appears well suited to address the problem of vascular smooth muscle cell proliferation. This method provides for sustained expression and conversion of the *prodrug* to its *toxic* form locally at the time of peak cell proliferation at concentrations that cannot be achieved by drug delivery. Despite the success of several pharmacological[27, 28] and antisense *oligonucleotide*[29] interventions in balloon injuries in the rat, the applicability of the rat carotid artery injury model to human vascular disease is uncertain. For example...

5/3,K/14 (Item 2 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01422864 SUPPLIER NUMBER: 14144560 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Anti-HIV properties of alpha-glucosidase inhibitor SC-48334, the active component of prodrug SC-49483. (Research Report)
Bryant, M.; Mueller, R.; Smidt, M.; Tiemeier, D.; Jacobs, G.; Platt, F.; Butters, T.; Karlsson, N.; Houseman, K.; Marr, J.
AIDS Weekly, p14(1)
July 26,
1993
PUBLICATION FORMAT: Newsletter ISSN: 1069-1456 LANGUAGE: English
RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 333 LINE COUNT: 00035

... 1993, in Berlin, Germany, "The N-linked glycans of the HIV envelope proteins are important for receptor binding, virus uptake and syncytia formation. Alteration of *oligosaccharide* addition, composition or processing leads to attenuation in HIV infectivity and cytopathicity due to aberrant folding, *oligomerization*, cleavage or transport of virion glycoprotein. SC-48334, n-butyl -deoxynojirimycin (BuDNJ), is an iminosugar which inhibits the endoplasmic reticulum a-glucosidase I resulting in biochemical modification of N-linked *oligosaccharides*. Inhibition of intestinal disaccharidases in vivo, however, can lead to carbohydrate malabsorption and diarrhea. *Prodrug* SC -49483 was developed to eliminate the GI side effects associated with oral administration of SC-48334. SC -49483 does not inhibit intestinal sucrase and...

...not fuse with uninfected lymphoid cells and virions released from the treated cells are noninfectious. SC-48334 is a potent (EC(50)=43 uM), non-*toxic* (TD(50)>5 mM) inhibitor of HIV replication and cytopathicity in human peripheral blood mononuclear cells, including monocytes/macrophages, infected with primary clinical isolates and...

5/3,K/15 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit

01140135 95615286
[Synthesis and evaluation of macromolecular mitomycin C derivatives.]

Synthese en evaluatie van macromoleculaire mitomycine C derivaten.
De marre A
Rijksuniversiteit te Gent, Belgium
Diss Abstr Int [C] 1994, 55 (4), ISSN 0419-4217
Languages: DUTCH
Document Type: THESIS
Record type: Completed

Many pharmacologically active compounds utilized in chemotherapy rapidly enter all cell types. This decreases their availability at the desired target tissue and sometimes causes *toxic* side-effects. Attachment of drugs to macromolecular carriers prevents uptake other than by the pinocytotic route, making them 'lysosomotropic', and affords a potential mechanism for...

...is coupled to a polymeric carrier, poly-(N-(2-hydroxyethyl)-L-glutamine) (PHEG), via peptide spacers. The aim of this work is to obtain macromolecular *prodrugs* of MMC which are stable and pharmacologically inactive during circulation but, after internalization, are degraded in the lysosomes with release of the active drug. We have synthesized PHEG conjugates of the cytotoxic agent MMC with different *oligopeptide* spacers. The influence of the amino acid sequence of the spacer on the hydrolytic and enzymatic stability of the macromolecular conjugate was investigated under different...

... release MMC very rapidly in presence of lysosomal proteases. Initial in vitro and in vivo studies indicate that the PHEG-spacer-MMC conjugates act as *prodrugs* of MMC. The conjugate itself is not *toxic* but causes a significant *toxicity* after hydrolysis of MMC. These results are promising for further evaluation of these conjugates in the development of a more effective chemotherapeutic treatment of cancer...
?